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Docket Number: 01D-0519,
Dockets Management Branch,
Division of Management Systems and Policy,
Office of Human Resources and Management Services,
Food and Drug Administration,
5630 Fishers Lane,
Room 1061, (HFA-305),
Rockville, MD 20852.

> Re: Cardiac Ablation Catheters Generic Arrhythmia Indications for
> Use; Draft Guidance for Industry.
> Federal Register Vol. 66 (December 7, 2001): Pages 63546 - 63547
> [FR Doc. 01–30330].
> Docket Number: 01D-0519

Dear Sir or Madam:

Boston Scientific Corporation/EP Technologies, Inc. (EPT) is writing to express general support for the proposed guidance document entitled Cardiac Ablation Catheters Generic Arrhythmia Indications for Use; Draft Guidance for Industry. As one of the market leaders in Cardiac Ablation Catheters, we appreciate the recognition FDA is giving Radiofrequency Catheter Ablation as a preferred treatment modality in the medical community for numerous cardiac arrhythmias. However, we do have a number of comments on the guidance, and are hereby requesting some additional information and clarification from the FDA. There are two critical sections of this Guidance, the definition of a conventional catheter, and the definitions and examples of tachycardias. EPT intends to limit this comment to those two sections.

Definition of Conventional Catheter

The requirements for classification as a conventional catheter should be modified for clarity to include: (changes are in italic text, with discussion below)

Based on the review of the medical literature, FDA defines conventional RF cardiac ablation catheters as those that have *all of* the following features:

1. Create endocardial *linear and focal* lesions,

> Discussion: Linear and focal lesions have been shown by the literature
> cited in the guidance to be safe and effective for the treatment of
> tachycardias in all chambers of the heart (Draft Guidance, page 3).

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The addition to this requirement of the italicized terms above would clearly indicate this.

2. Single 4-5 mm ablation *tip* electrode,

> Discussion: There are several different types of electrodes capable of delivering RF energy; for example, coil and tip electrodes. The requirement should be clarified to address this.

3. Temperature sensing capability,

4. Not irrigated or cooled,

> Discussion: Cooled catheters have been approved via PMA and have been on the market for several years. Literature reports the safe and effective use of cooled catheters for the treatment of ventricular tachyarrhythmias, as well as other cardiac arrhythmias (see bibliography). (Draft Guidance page 4 and reference 16) Medical literature has established the creation of larger lesions with lower occurrence of impedance rise.
>
> Additionally, cooled ablation catheters are the only cardiac catheters currently approved through the PMA process specifically for the treatment of Ventricular Tachycardia.

5. "Steerable" (i.e., catheter has a manually-deflectable tip),

6. Placed percutaneously, and

7. Designed to deliver a maximum of *60W* Radiofrequency power to the endocardium *in any chamber of the heart*.

> Discussion: There are currently both 50 and 60 W generators approved and in the marketplace. The recommended increase in wattage is minimal, and clinical data has not been required for this change in the past. Additionally, the literature data for this guidance were chosen to demonstrate the safety and effectiveness of using conventional RF catheters to create either focal or linear lesions in any of the four chambers of the heart (Draft Guidance, page 3).

Definition of Tachyarrhythmias

Tachyarrhythmias can be classified in numerous ways, but broadly there are two categories corresponding to the location of the arrhythmia within the heart. If the initiation of the arrhythmia is in the atria, the upper chambers of the heart, it is classified as an atrial tachycardia; if it occurs in the ventricles, the lower chambers of the heart, it is classified as a ventricular tachycardia. Within these two broad categories, there are numerous defined arrhythmias which have been reported and well-characterized in the medical literature. Additionally, an arrhythmia may be classified according to the type
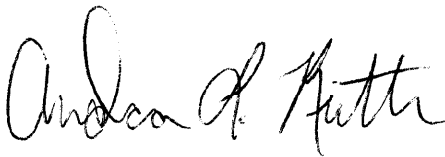
and location of its trigger (i.e. focal or idiopathic or macro-reentrant). EPT requests that FDA clarify the citation of these four arrhythmias as illustrative only, and/or expand the listing to include a more definitive listing of arrhythmias. For Example:

* Atrial Tachycardias can include:
    * atrial tachycardia occurring due to macro-reentrant circuits, and
    * focal atrial tachycardia.
* Supra-ventricular Tachycardia (SVT),
    * Atrioventricular (AV) Reentrant Tachycardias,
    * AV Nodal Reentrant Tachycardia, and
    * Atrial Tachycardias with Rapid Ventricular Response,
* Wolfe-Parkinson-White Syndrome (WPW),
* Inappropriate Sinus Tachycardias,
* Atrial Flutter (AF), and
* Atrial Fibrillation (A Fib).
* Ventricular Tachycardias.

In conclusion, EPT believes that if the FDA adopts the recommendations outlined above, the clarity of the resulting final guidance will assure the accurate implementation and preparation of appropriate supplements concerning cardiac ablation catheters, and that the supplemental approval process will thereby be streamlined and improved. Additionally, the dissemination of unbiased and balanced information regarding the use of Radiofrequency Ablation as an approved method for the treatment of cardiac arrhythmias will be facilitated. EPT appreciates the opportunity to comment on this important Proposed Guidance and looks forward to continuing to work with the FDA on its successful implementation.

Sincerely,

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Prospective Randomized Comparison of Cooled RF versus Standard RF Energy For Ablation of Typical Atrial Flutter

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Abstract

Background In patients with type I atrial flutter (AFL), conventional RF ablation may require up to 50 or more lesions before isthmus block is achieved. In this prospective, randomized study, we tested the hypothesis that the Cooled RF catheter ablation is safe and facilitates the achievement of bidirectional isthmus block with fewer RF applications than with standard ablation for typical AFL.

Methods and Results Isthmus ablation was performed in 59 patients (40 males, 64 ± 14 years) with type I AFL using Standard RF (n=31) or Cooled RF (n=28) ablation catheters, with crossover after 12 unsuccessful RF applications. The endpoint was the achievement of bidirectional isthmus block or a total of 24 unsuccessful RF applications. After the first 6 RF applications, bidirectional isthmus block (BIB) was demonstrated in 7 of 31 (23%) Standard RF and 7 of 28 (25%) Cooled RF patients (P=NS). Following 12 RF applications, BIB had been demonstrated in 17 of 31 (55%) Standard RF patients and 22 of 28 (79%) Cooled RF patients (p<0.05). After the remaining patients crossed over to the alternate RF ablation system and underwent 6 more RF applications, BIB had been demonstrated in 23 of 31 (74%) Standard RF and 24 of 28 (86%) Cooled RF patients (p=NS). After the final 6 RF applications of the protocol, BIB had been demonstrated in 27 of 31 (87%) Standard RF and 25 of 28 (89%) Cooled RF patients (p=NS). Isthmus block could not be achieved within 24 RF applications in 3 Standard RF and 3 Cooled RF patients. Mean temperatures for Cooled RF were lower than for Standard RF (38.5 ± 6.98 °C versus 57.2 ± 7.42 °C, P< .0001). Peak temperatures were also lower for Cooled RF compared to

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Standard RF (45.7 ± 22.7 °C versus 63.4 ± 9.87 °C, P<.0001). Importantly, mean power delivered was significantly higher for Cooled RF compared to Standard RF (42.3 ± 9.48 W versus 34.0 ± 14.0 W, P<.0001). Peak power achieved was similar for both Cooled RF and Standard RF. There were no serious complications for either RF ablation system.

Conclusions In patients with type I AFL, ablation with the Cooled RF catheter is as safe as and facilitates creation of bidirectional isthmus block more rapidly than Standard RF ablation.

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Condensed Abstract

This prospective, randomized study of atrial flutter (AFL) patients compared Cooled versus Standard RF ablation for safety and efficacy in achievement of bidirectional isthmus block (BIB). Fifty-nine patients (40 males, 64 ± 14 years) underwent isthmus ablation using Standard RF (n=31) or Cooled RF (n=28) ablation, with crossover after 12 RF applications to endpoints of BIB or 24 unsuccessful RF applications. After 6 RF applications, BIB achievement was similar for both groups. Following 12 RF applications, 17 (55%) Standard RF and 22 (79%) Cooled RF patients had BIB (p<0.05). At protocol end, 27 (87%) Standard RF and 25 (89%) Cooled RF patients had BIB (p=NS). Mean and peak temperatures were lower for Cooled than Standard RF. Mean power was higher for Cooled than Standard RF (42.3 ± 9.48 W versus 34.0 ± 14.0 W, P<.0001). There were no serious complications for either group. Cooled RF ablation is safe and facilitates creation of BIB.

Introduction

Catheter ablation has become widely performed as curative treatment of typical atrial flutter (AFL) (1-6). Although the achievement of bidirectional isthmus conduction block has been demonstrated to result in the lowest recurrence of AFL following radiofrequency (RF) ablation (2,7-10), in some patients, bidirectional isthmus block cannot be achieved (9,11). It has been proposed that these cases may result from thick atrial tissue in this region of the heart, which may be more than 1 cm in thickness (12).

Given the ability of saline-cooled catheters to create larger ablative lesions compared to conventional RF systems (13), we tested the hypothesis that the Chilli® Cooled RF ablation system (Cardiac Pathways Corporation) facilitates catheter ablation of AFL as compared with a conventional RF ablation system and is safe when used to treat this arrhythmia.

Methods

Patient Population

Fifty-nine consecutive patients from three centers referred for RF ablation of type I AFL were included in the study. Patients who had previously undergone isthmus ablation were excluded. There were 40 males and 19 females, with a mean age 64 ± 14 years. Thirty-seven patients were resistant to or intolerant of drug therapy for AFL, despite treatment with a mean of 1.35 ± 0.63

antiarrhythmic drugs, including amiodarone in 19 patients. The remaining 22 patients preferred not to undergo treatment with antiarrhythmic agents. Thirty-two patients also had a prior history of atrial fibrillation. Nineteen patients had no underlying structural heart disease. The remaining patients had structural heart disease: ischemic (n=23), hypertensive (n=9), idiopathic dilated cardiomyopathy (n=4), valvular (n=3), and congenital (n=1). The mean ejection fraction was 49 ± 15 %. The New York Heart Association functional class was 1.6 ± 0.7. Informed consent was obtained from all patients. The study protocol was approved by the respective Institutional Review Boards of each of the participating centers.

Electrophysiologic Testing

All patients gave written informed consent prior to electrophysiologic testing. Four multipolar electrode catheters (2-mm interelectrode spacing) were inserted percutaneously into the right and left femoral veins. Three of the catheters were advanced to the right ventricular apex, His bundle region, and the coronary sinus. A 7F deflectable 20-pole catheter (Halo catheter, Cordis Webster) was positioned around the tricuspid annulus to record atrial activation close to the lateral and posterior tricuspid annulus.

In patients in sinus rhythm at the onset of the procedure, AFL was induced by programmed atrial stimulation with up to 2 extrastimuli. If AFL was not induced, atrial burst pacing was performed at progressively shorter cycle lengths to 150 ms or atrial refractoriness, whichever was reached first. If the patient was in AFL at the start of the electrophysiology test, atrial pacing was performed at

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progressively shorter cycle lengths between 300 and 150 ms to terminate AFL. Once AFL was induced, isthmus dependence was confirmed by demonstration of concealed entrainment.

Radiofrequency Ablation and Study Design

Once the diagnostic study was completed and a decision had been made to create isthmus block, the patients were then randomized to either Standard or Cooled RF as the initial ablation system.

For those patients initially randomized to Standard RF, a conventional 4 mm ablation catheter of the investigator's choice was used to apply the first 12 RF lesions. Ablation was performed in temperature control mode for 60 seconds with a set point of 70 °C.

The internally perfused Chilli® ablation catheter (Cardiac Pathways Corporation) was used for the first 12 lesions in those patients initially randomized to Cooled RF. Sterile normal saline was infused at 0.6 ml/sec through a pair of inner lumens in order to cool the catheter tip. The temperature of the electrode was monitored with a thermocouple at the catheter tip. The target catheter tip temperature was 45 °C. Power was initiated at 20 watts and increased gradually to achieve the target temperature. Ablation was performed for 60 seconds.

During each application of RF energy with either Standard or Cooled RF, power, temperature and impedance were monitored continuously. RF energy delivery was terminated if an audible pop or an impedance rise (defined as a

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25 ohm rise) were noted, and the catheter was removed for inspection of the tip for presence of coagulum or char formation.

After 6 linear sequential (point-by-point) applications of energy from the tricuspid annulus to the inferior vena cava, bidirectional isthmus conduction block was assessed using standard techniques (8,14). If bidirectional conduction block was not observed, 6 additional applications of energy were given and conduction block was again evaluated. If conduction block was not achieved using 12 applications of energy, then cross over to the alternate RF system occurred. Following delivery of 6 more applications, testing for bidirectional isthmus block was again performed. If there was still evidence of isthmus conduction, 6 final applications of RF energy were given. If conduction block was still not present after 24 applications of energy were given, then the study protocol was considered to have ended and it was up to the investigator whether to continue giving RF applications using either system.

Where possible, ablation was performed in sinus rhythm in order to allow for greater convective catheter cooling. Anticoagulation was not given routinely during the procedure. Echocardiograms were obtained at least 60 days prior to the procedure and then following the procedure to determine if there was evidence for pericardial effusion or pericardial tamponade.

Follow-up

In order to compare the long-term efficacy of Cooled versus Standard RF ablation, patients were followed prospectively from the time of RF ablation.

Follow-up was obtained by outpatient clinic visits or by telephone interview of patients, their families or their referring physicians.

Statistical Analysis

All data are expressed as mean ± SD and were all two-tailed. Statistical analyses were performed using Statview version 5.0 for Macintosh (SAS Institute, Inc.) software. Comparisons between patients undergoing ablation initially using Cooled RF energy and those using Standard RF energy were done using the unpaired Student's *t*-test. Comparisons between Cooled and Standard RF to determine any differences in creation of bidirectional isthmus block after 6 and 12 RF applications were performed with contingency table analysis. Event-free rates for AFL recurrence were determined by Kaplan-Meier cumulative survival analysis. The differences between survival curves for Cooled versus Standard RF were determined by the Mantel-Cox logrank procedure. Statistical significance for all tests was accepted at the P 0.05 level.

Results

Comparison of Efficacy of Atrial Flutter Ablation

Of the 59 patients enrolled in the study, 31 patients were randomized to Standard RF ablation and 28 patients to Cooled RF ablation initially (Figures 1 and 2). There were no differences in baseline clinical characteristics, with the

exception of ejection fraction, which was lower in those undergoing ablation using Cooled RF initially (Table 1). After the first 6 RF applications, bidirectional isthmus block was demonstrated in 7 of 31 (23%) Standard RF and 7 of 28 (25%) Cooled RF patients (P=NS). After 6 more RF applications in the remaining patients, bidirectional isthmus block had been demonstrated in 17 of 31 (55%) Standard RF and 22 of 28 (79%) Cooled RF patients (p=0.05). The results of RF ablation in patients requiring crossover to the alternate RF ablation system are shown in Figures 1 and 2 for Standard RF and Cooled RF patients, respectively. Bidirectional isthmus block could not be achieved with 24 or fewer RF applications in 4 Standard RF and 3 Cooled RF patients (P = NS). However, in these 7 patients who required additional RF applications beyond the initial 24 RF applications allotted by the protocol, bidirectional isthmus block was eventually achieved in 3 Standard RF and 2 Cooled RF patients using the ablation system of the investigator's choice. These additional RF applications were successfully given using the Cooled RF catheter in all 3 Standard RF patients and 1 Cooled RF patient. The other Cooled RF patient eventually developed isthmus block using a conventional RF catheter. The single Cooled RF patient in whom bidirectional isthmus block could not be demonstrated underwent AV junction ablation and permanent pacemaker implantation.

Comparison of Ablation Parameters

The comparisons between ablation parameters for Cooled RF versus Standard RF are shown in Table 2. The mean and peak temperatures were lower

for Cooled RF than for Standard RF ablation. Importantly, mean power delivered was higher with Cooled RF than Standard RF. Maximum impedance was higher for Cooled RF than for Standard RF. In the Cooled RF group, there were 43 impedance rises that resulted in automatic power shutoff of the ablation catheter, 4 of which were associated with audible pops. The other 39 impedance rises were not associated with audible pops, and none of these impedance rises were associated with coagulum formation. In contrast, only 6 impedance rises were noted in the Standard RF group. However, 2 of these were associated with coagulum formation on the catheter tip electrode.

Follow-up

Event-free rates for AFL recurrences are shown in Figure 3. During a mean follow-up period of 12.8 ± 3.76 months, there were 2 recurrences of AFL in the Cooled RF group and 4 recurrences in the Standard RF group (p = 0.61) There were five patients who had atrial fibrillation during the follow-up period, 4 from the Cooled RF group and 1 from the Standard RF group.

Safety of Atrial Flutter Ablation

There were no cases of pericardial effusion, tamponade or other major complications for either Cooled or Standard RF patients.

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Discussion

Major findings

The results of this study demonstrate that catheter ablation of AFL with Cooled RF energy can be accomplished with equal safety as compared with Standard RF energy and that Cooled RF energy facilitates catheter ablation of AFL. Whereas isthmus block was achieved in 55% of patients after 12 RF applications using Standard RF energy, isthmus block was achieved in 79% of patients after 12 Cooled RF applications. Cooled RF ablation resulted in significantly lower mean and peak temperatures and allowed significantly higher mean power delivery without formation of coagulum when compared to Standard RF ablation.

Conventional RF ablation of AFL

Typical AFL is a macroreentrant tachycardia that has been shown to be critically dependent on conduction through the isthmus between the tricuspid annulus and the inferior vena cava (1-3).

Catheter ablation of AFL was first reported in 1986 and was performed by employing cryosurgery in the region of the coronary sinus ostium (15). Subsequently, catheter ablation of AFL using DC shock energy delivered in the low posteroseptal right atrium was reported, with a success rate of approximately 50% (16). Direct current energy has since been abandoned and replaced by RF

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ablation of the cavotricuspid isthmus has become widely performed as curative treatment of typical AFL (1-6).

Ablation of AFL was initially performed by targetting a focal zone of slow conduction (4) and fragmented electrograms (5). Successful ablation was determined by AFL termination during RF delivery and acute noninducibility. It was later shown that the endpoint of demonstration of bidirectional isthmus conduction block during sinus rhythm resulted in the lowest rates (9%-16%) of AFL recurrence (2,7,8,17-19).

In most series, the reported acute efficacy for RF catheter ablation of AFL exceeds 85% (1-10). The mean number of RF applications required to achieve bidirectional isthmus block have ranged from two to thirty-two (2,9,11,19,20), with individual requirements of up to 82 lesions (10). Thus, in some patients, conventional RF ablation may require many lesions before bidirectional isthmus block is achieved. Moreover, in a subset of patients, bidirectional isthmus block cannot be achieved using conventional RF catheters (9.11,20). It has been proposed that the inability to achieve a complete line of block in some patients may reflect both thickened myocardial tissue (12) and the length of the isthmus, which commonly measures 2 to 2.5 cm in length, and may reach up to 6 cm in some cases (21). Thus, there is a need for employing new techniques or technologies that will facilitate the creation of bidirectional isthmus block without compromising safety.

Alternative RF Ablation of AFL

It is well known that deeper ablation lesions can be obtained by increasing the RF power, since this increases both the volume of resistive heating and the depth of passive conductive heating. However, because coagulation necrosis at the tissue-electrode interface results in a rise in impedance once temperatures reach 100 , the degree to which RF power, and thus lesion size, can be increased is limited (22,23). Recently, methods for improved cooling of the electrode have been developed to allow delivery of a constant, more stable, and higher amount of RF power. These include the use of larger (8 mm) electrodes (9,24,25), which receive greater convective cooling by the blood, and saline-irrigated electrode tips, in which the electrode is actively cooled (13,26). By cooling the electrode-tissue interface, higher RF power can be delivered without an impedance rise. This significantly increases the volume of resistive heating, which in turn would increase lesion depth (13,26). The use of these catheters in humans has resulted in higher success rates for selected arrhythmias, including ventricular tachycardia and isthmus-dependent AFL (27-30).

Comparison with Prior Studies

The results of this study confirm and extend those of prior investigators. The first clinical use of an irrigated-tip cathteter for resistant AFL was described by Jais et al in 13 patients, in whom bidirectional isthmus block was not achieved after >21 RF applications (11). The use of this catheter (Cordis Webster, Medtronic Inc.) resulted in bidirectional isthmus block in 12 of 13 patients, with no

adverse events. Subsequently, in a prospective, randomized study, Jais et al (30)

compared an irrigated-tip catheter (Cordis Webster Thermocool) with a

conventional-tip catheter for ablation of common AFL in 50 patients. The number

of RF applications, procedure duration, and x-ray exposure were significantly

higher with conventional than with the irrigated-tip catheter. In addition, the

irrigated-tip catheter was as safe as the conventional ablation catheters.

Consistent with the findings of Jais and colleagues (30), the present study

demonstrated the positive effects of cooling the electrode-tissue interface, as

evidenced by the lower mean and peak temperatures and higher mean power

delivered. These findings translated into earlier achievement of bidirectional

isthmus block as compared to Standard RF ablation without compromising

safety.

Important differences of this study include the fact that our primary

endpoint was earlier achievement of bidirectional isthmus block than the

alternate RF catheter system, whereas Jais et al (30) had primary endpoints of

flutter termination and demonstration of bidirectional isthmus block. Our study

also employed the internally perfused Cooled RF ablation system as compared

with the irrigated-tip catheter used by Jais and colleagues. Currently, only the

Cardiac Pathways Cooled RF system is available for use in the United States.

Safety of Cooled RF Ablation

The excellent safety results achieved in this study are reassuring. Among

the 59 randomized patients, catheter ablation with Cooled RF either as first line

therapy or after crossover was performed in 42 patients. No complications occurred in any of these patients. In fact, the only cases of coagulum formation occurred in 2 patients during ablation with conventional RF catheters. It is important to note that the safety of using a saline irrigated-tip catheter in the flutter isthmus has now been demonstrated in at least three studies, including the present one (11,30).

Limitations

There are two main limitations to this study. First, data concerning procedure and fluroscopy times were not obtained in this study. Second, the precise location of lesions was not tracked using a 3-D system.

Clinical Implications

This study adds further evidence that saline-cooled RF ablation catheters are as safe as and are more effective than conventional RF ablation catheters for creation of bidirectional isthmus block for typical AFL. This type of ablation may be of particular value for those patients with resistant AFL who have a broad and/or thick isthmus.

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Figure Legends

Figure 1.   Results of Standard RF ablation for atrial flutter in achieving bidirectional isthmus block. RFs, radiofrequency applications.

Figure 2.   Results of Cooled RF ablation for atrial flutter in achieving bidirectional isthmus block. RFs, radiofrequency applications.

Figure 3.   Survival curves comparing event-free rates of atrial flutter recurrence for Standard RF and Cooled RF groups.
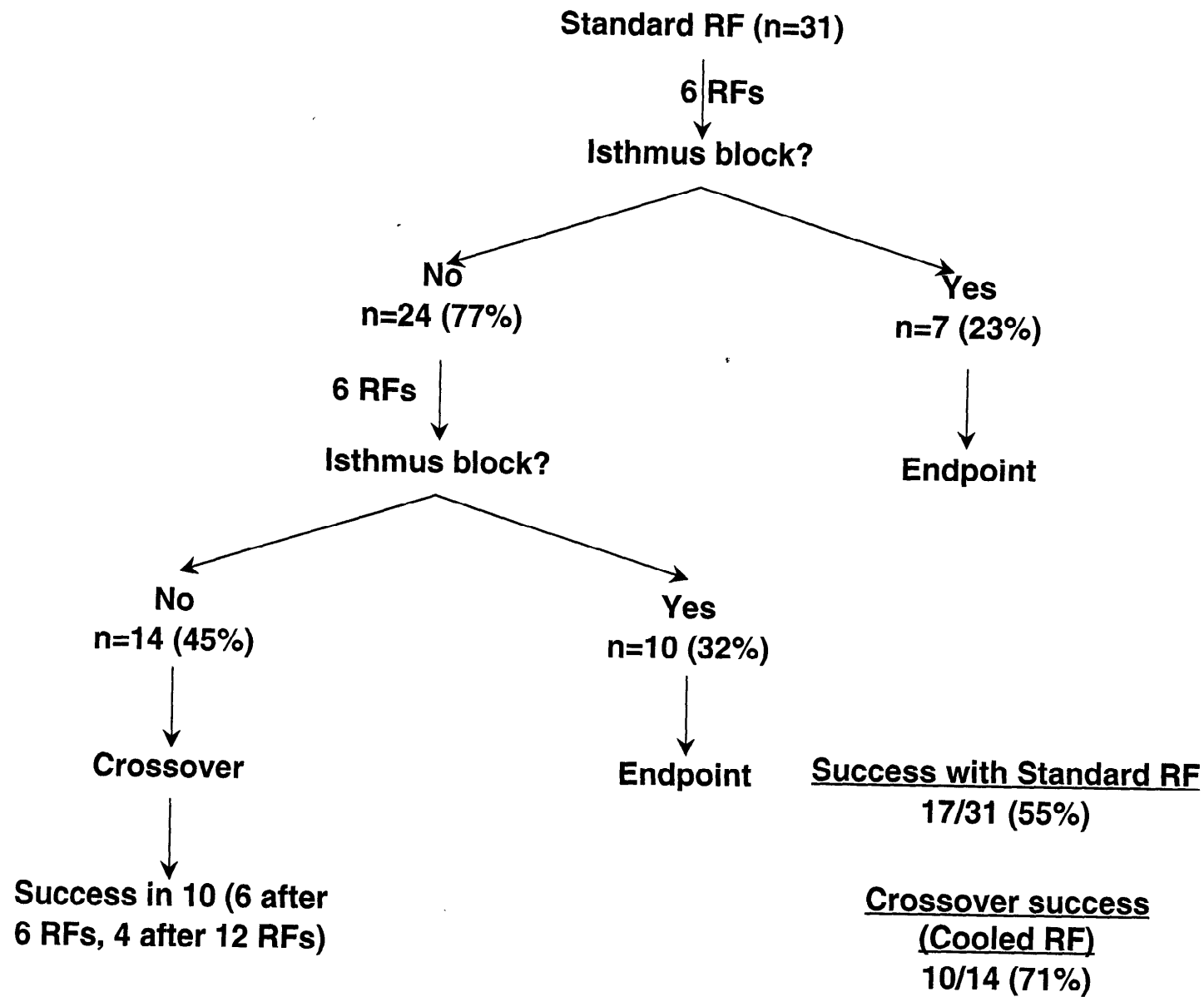
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Standard RF (n=31)
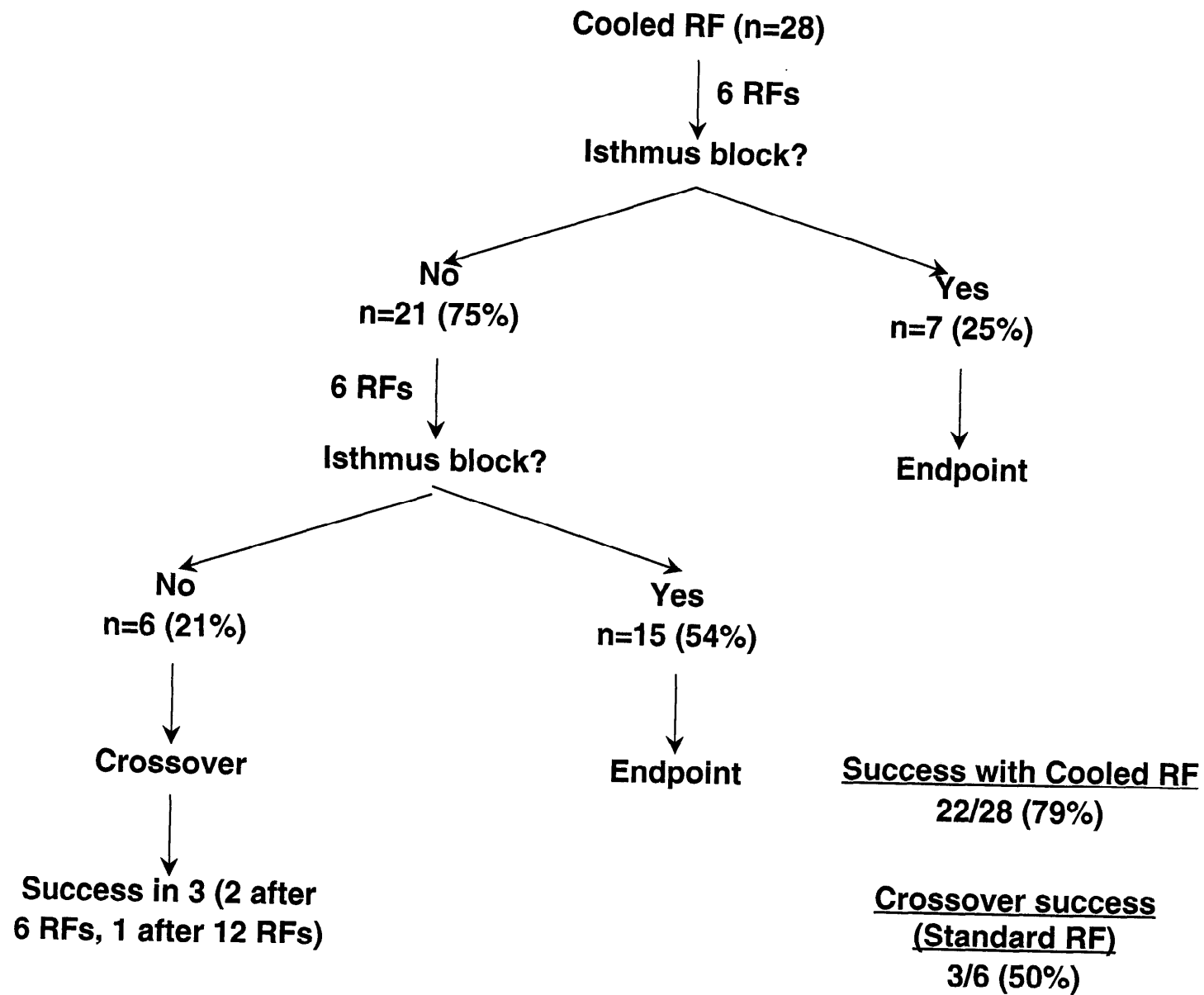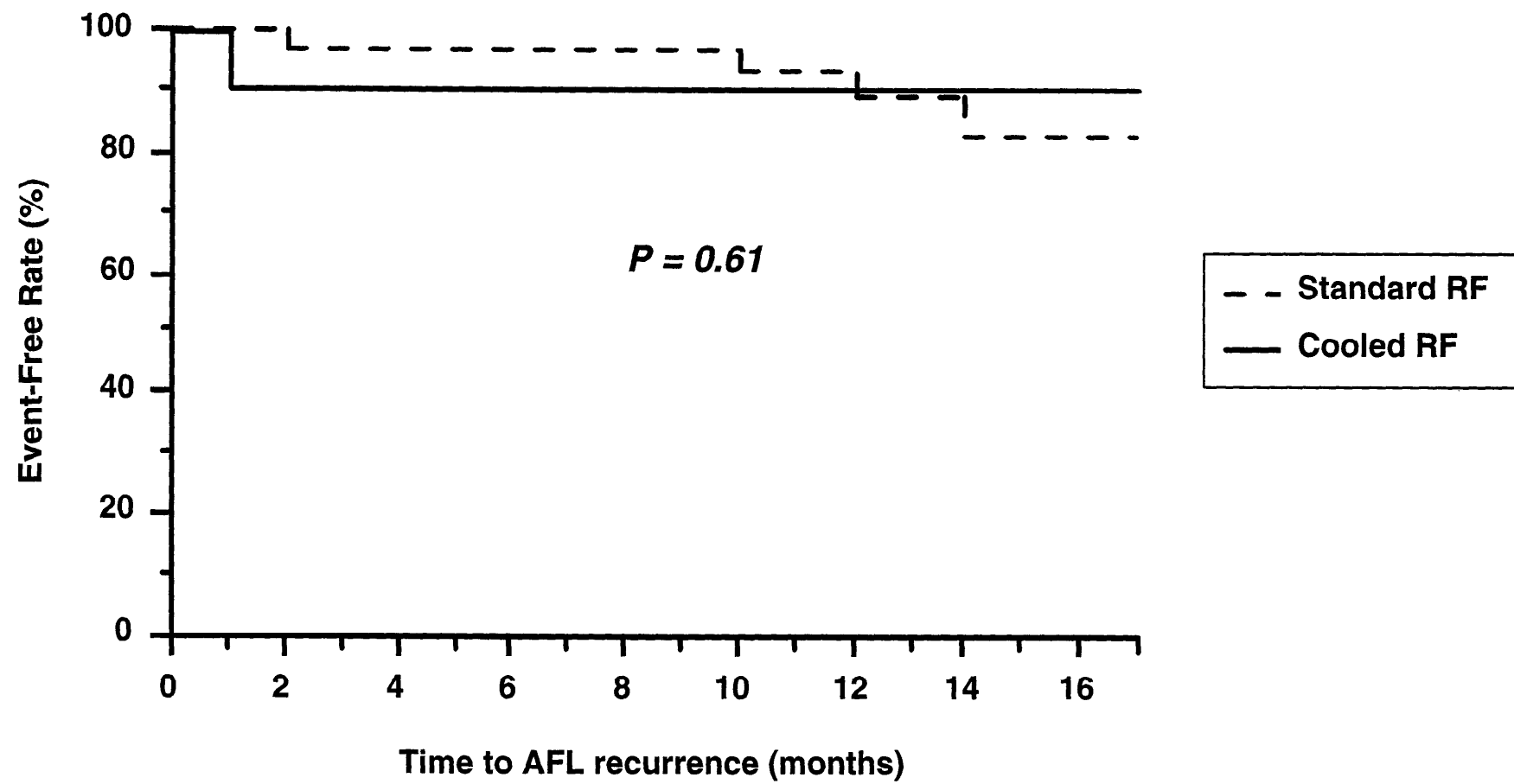
6 RFs

Isthmus block?

No
n=24 (77%)

Yes
n=7 (23%)

6 RFs

Isthmus block?

Endpoint

No
n=14 (45%)

Yes
n=10 (32%)

Crossover

Endpoint

Success with Standard RF
17/31 (55%)

Success in 10 (6 after
6 RFs, 4 after 12 RFs)

Crossover success
(Cooled RF)
10/14 (71%)

Figure 1

Cooled RF (n=28)

6 RFs

Isthmus block?

No
n=21 (75%)

Yes
n=7 (25%)

6 RFs

Isthmus block?

Endpoint

No
n=6 (21%)

Yes
n=15 (54%)

Crossover

Endpoint

Success with Cooled RF
22/28 (79%)

Success in 3 (2 after
6 RFs, 1 after 12 RFs)

Crossover success
(Standard RF)
3/6 (50%)

Figure 2

P = 0.61

Standard RF
Cooled RF

Event-Free Rate (%)

100
80
60
40
20
0

0   2   4   6   8   10   12   14   16

Time to AFL recurrence (months)

Figure 3

TABLE 1. Clinical Characteristics of Patients

	All Patients	Cooled RF	Standard RF	P-value
$N =$	59	28	31	NS
Males	40	20	20	–
Age (years)	63 ± 14	67±15	63 ± 11	NS
EF (%)	49 ± 15	44 ± 17	51 ± 12	0.04
AAD's Failed	.85 ± .83	.71 ± .85	.98 ± .80	NS

Data are expressed as mean ± standard deviation or number of patients.
AAD, antiarrhythmic drugs. EF, ejection fraction. NS, not significant.

TABLE 2. Radiofrequency Ablation Parameters

	Standard RF	Cooled RF	P-value
Mean Temperature (°C)	57.2 ± 7.42	38.5 ± 6.98	< .0001
Peak Temperature (°C)	63.4 ± 9.87	45.7 ± 22.7	<.0001
Mean Power (W)	34.0 ± 14.0	42.3 ± 9.48	<.0001
Peak Power (W)	42.7 ± 10.5	43.1 ± 9.06	NS
Maximum Impedance (}	108 ± 28.1	135 ± 67.4	<.0001
Mean # of lesions	13.7 ± 7.19	14.7 ± 10.9	NS
Total # of lesions*	408	411	NS
Impedance rises	6	43	<.0001
Audible pop	0	8	–
-with impedance rise	0	4	–
-without impedance rise	0	4	–
Coagulum	2	0	–

Data are expressed as mean ± standard deviation or number of patients.
*Including crossover and additional out-of-protocol lesions.
NS, not significant.

Temperature Monitoring During Radiofrequency Catheter Ablation Procedures Using Closed Loop Control

Hugh Calkins, MD; Eric Prystowsky, MD; Mark Carlson, MD; Lawrence S. Klein, MD; J. Philip Saul, MD; Paul Gillette, MD; the Atakr Multicenter Investigators Group

Background The purpose of this study was to evaluate electrode temperatures obtained using a radiofrequency ablation system that incorporates closed loop feedback control to achieve preset target electrode temperatures and to determine if closed loop temperature control results in a lower incidence of developing a coagulum.

Methods and Results Two hundred seventy patients underwent catheter ablation of atrioventricular nodal reentrant tachycardia, an accessory pathway, and/or the atrioventricular junction using an ablation system incorporating closed loop feedback control. Forty-five patients underwent catheter ablation in the power control mode in which power output was fixed, and 225 patients underwent catheter ablation in the temperature control mode. A coagulum occurred during 0.8% of radiofrequency applications in the temperature control mode versus 2.2% in the power control mode ($P<.01$). Electrode temperatures were within 10°C of the targeted temperature during 35% of applications in the temperature control mode. Ability to achieve the targeted electrode temperature

was related to the target, with radiofrequency energy applications at the atrioventricular junction resulting in the highest temperatures (70±12°C) and those for ablation of the atrioventricular node the lowest (59±11°C, $P<.001$), using a maximum of 50 W of power for both. Electrode temperatures were higher during ablation of left free wall and posteroseptal pathways than during ablation of right free wall and septal pathways. The mean and minimum temperatures associated with success were 64±12°C and 44°C, respectively. Overall, the electrode temperatures at successful and unsuccessful ablation sites did not differ ($P>.05$).

Conclusions Temperature monitoring with closed loop control of power output facilitates radiofrequency catheter ablation procedures by minimizing the probability of developing a coagulum while ensuring maximum lesion formation. (*Circulation.* 1994;90:1279-1286.)

Key Words • radiofrequency • Wolff-Parkinson-White syndrome • coagulation • catheter ablation

R adiofrequency catheter ablation has emerged as an important therapeutic tool for management of patients with sustained supraventricular arrhythmias.[1-3] Tissue temperature is critically related to the success or failure of these procedures because thermal injury is the primary mechanism of myocardial injury.[4-7] For irreversible injury to occur, a tissue temperature of approximately 50°C must be achieved.[4,7] Although lesion size increases with increasing temperature at the electrode-tissue interface, 100°C represents the upper limit of achievable tissue temperatures. Temperatures ≥100°C result in the development of a coagulum on the electrode tip, which leads to an abrupt rise in impedance, an abrupt fall in current delivery to tissue, and a marked decrease in tissue heating.[7,8] Furthermore, if a coagulum develops, the ablation catheter must be removed, cleaned, and repositioned, necessitating additional catheter manipulation and additional fluoroscopy time. Coagulum formation is also a potential source of embolization. Because of the importance of temperature during radiofrequency catheter ablation procedures, temperature monitoring has been

proposed as a technique to facilitate effective catheter ablation by assuring adequate lesion formation, optimizing lesion size, and preventing coagulum formation.[7-9]

The purpose of the present study was to evaluate electrode temperatures obtained using a radiofrequency catheter ablation system that incorporates closed loop feedback control to achieve preset target electrode temperatures and to determine if closed loop temperature control results in a lower incidence of coagulum formation. Particular attention is focused on the relation between electrode temperature and the ablation target, approach (atrial versus ventricular), and result.

Methods

Characteristics of Patients

The subjects of this study were 270 consecutive patients who underwent an attempt at catheter ablation of atrioventricular nodal reentrant tachycardia, an accessory pathway, and/or the atrioventricular junction using a radiofrequency catheter ablation system incorporating closed loop feedback control. Each patient gave written informed consent according to a protocol approved by the Institutional Review Board of each participating institution. The mean patient age was 39±22 years (±SD; range, 0.75 to 90 years). There were 137 women and 133 men.

Two hundred sixty-seven patients underwent catheter ablation of a single accessory pathway or other ablation target, and three patients had two ablation targets. Ninety-two patients underwent catheter ablation to treat atrioventricular nodal reentrant tachycardia, and 35 patients underwent catheter
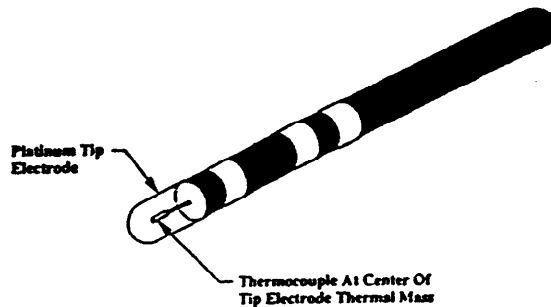
Fig 1. Schematic drawing of the 7F ablation catheter used in this study. Shown is the thermocouple positioned at the center of the platinum tip electrode.

ablation of the atrioventricular junction to cause complete atrioventricular block. Catheter ablation was attempted for a total of 146 accessory pathways. Seventy-six pathways were located on the left free wall, 28 were right free wall, 33 were posteroseptal, and 9 were septal (anteroseptal or midseptal).

Electrophysiological Testing and Catheter Ablation

Each patient underwent a standard diagnostic electrophysiology test in conjunction with the catheter ablation procedure. The number and type of electrode catheters used varied based on physician preference and the type of arrhythmia. Once the tachycardia mechanism was defined. catheter ablation was performed using standard techniques. Patients in whom the mechanism of the tachycardia was determined to be neither atrioventricular nodal reentrant tachycardia nor an accessory atrioventricular connection and in whom ablation of the atrioventricular junction was not indicated were excluded from the protocol.

Catheter ablation to cure atrioventricular nodal reentrant tachycardia was performed using the posterior (slow pathway) approach. Selection of target sites was based on local electrograms, fluoroscopic catheter position, or both. Catheter ablation of left free wall and left posteroseptal accessory pathways was performed using either the transseptal or retrograde aortic approach, based on physician preference. Right free wall, right posteroseptal, and right mid and anterior septal accessory pathways were ablated using a catheter positioned from the inferior or superior vena cava. Ablation of the atrioventricular junction was performed with a catheter positioned from the inferior vena cava.

In each patient, catheter ablation was initially performed using an investigational ablation system in which power output was preset or automatically varied to achieve target electrode temperatures using closed loop control. The ablation system was used in the temperature control mode in the initial 100 patients, in the power control mode in the subsequent 45 patients, and thereafter in the temperature control mode. If successful ablation was not achieved, an alternate ablation system could be used at any point during the ablation procedure, based on physician preference. Data obtained after switching to an alternate ablation system were excluded from analysis.

Ablation System

In the present study, catheter ablation was initially attempted with a 7F quadripolar electrode catheter (RF Ablatr, Medtronic CardioRhythm) with an omnidirectional deflectable shaft and a 4-mm distal electrode. A thermocouple was incorporated into the distal electrode to allow for temperature monitoring (Fig 1). Radiofrequency energy was produced by a power supply that delivered a continuous unmodulated sinusoidal output at 482 kHz (Atakr, Medtronic CardioRhythm). When operated in the temperature control mode, the power supply automatically modulates the amount of power delivered

(range, 0.5 to 50 W) so that the tip temperature approaches but does not exceed the selected target temperature (40° to 95°C) by >5°C. When operated in the power control mode, the power output is kept constant. In either mode, power output is automatically shut down if the impedance exceeds 250 Ω (impedance shutdown) or if the electrode temperature exceeds 100°C (temperature shutdown). A temperature shutdown will also occur if the electrode temperature exceeds the target temperature by >8°C in the temperature control mode. At each site, radiofrequency energy was delivered for 10 to 30 seconds or until dislodgment of the ablation catheter. When used in the temperature control mode, the initial target temperature was set at 70°C. If desired, the target temperature could be increased in increments of ≤5°C to a maximum of 95°C and additional applications of radiofrequency energy delivered. When used in the power control mode, the initial power output was set at 25 W. If desired, the power output could be increased in ≤5-W increments.

Data Analysis

A Fisher's exact test was performed to compare the incidence of automatic radiofrequency generator shutdowns and coagulum formation during radiofrequency energy applications in the power control mode versus the temperature control mode and to evaluate the association between target temperature and the incidence of power shutdowns and coagulum formation. Electrode temperature data were obtained only during catheter ablation in the temperature control mode. For each application of radiofrequency (electrode temperature) energy, the maximum achieved electrode temperature was recorded. To evaluate the relation between electrode temperature, the ablation target, and the ablation result, four indices of electrode temperature were compared: maximum temperature, the difference between targeted temperature and maximum temperature, the proportion of radiofrequency applications during which a peak temperature of ≥50°C was achieved, and the proportion of radiofrequency applications during which the maximum electrode temperature was >5°C below the target temperature. The relations between temperature target and approach (atrial versus ventricular) were compared using ANOVA or a contingency table analysis where appropriate. The maximum temperature achieved during successful versus unsuccessful applications of radiofrequency energy was compared using a nonpaired t test. Successful ablation sites were defined as those that resulted in ablation of the targeted arrhythmia during the ablation procedure. Transiently successful ablation sites that were associated with recurrence of conduction during a 30-minute observation period were excluded from analysis. A late recurrence was defined as recurrence of the targeted arrhythmia either spontaneously or during the 1-month follow-up electrophysiology study. Continuous variables are expressed as mean±1 SD. In all cases, $P<.05$ was considered significant.

Results

Clinical Results

The initial catheter ablation session using the investigational ablation system was successful in 83 of 92 (90%) patients with atrioventricular nodal reentrant tachycardia, 29 of 35 (83%) patients undergoing ablation of the atrioventricular junction, and 120 of 146 (82%) accessory pathways. Sixteen patients with an accessory pathway had an initially unsuccessful ablation session and underwent a second ablation session using the same system. Catheter ablation was successful in 9 of these 16 patients. Overall, 129 of 146 (88%) accessory pathways were successfully ablated with the investigational system. The mean number of applications of

TABLE 1. Relation Between Control Mode and the Incidence of Developing a Power Shutdown and/or Coagulum

Control Mode	Impedance Shutdown	Temperature Shutdown	Coagulum	Total*
Temperature (n=1948)	8 (0.4%)	19 (1%)	16 (0.8%)	38 (2%)
Power (n=662)	41 (6.2%)	35 (5.3%)	15 (2.2%)	79 (12%)
P	.0001	.0001	.006	.001

*Total number of radiofrequency energy applications during which an impedance shutdown, temperature shutdown, and/or a coagulum occurred.

radiofrequency energy per ablation target was 9±8 (median, 8; range, 1 to 41).

Twenty-eight of 32 patients who underwent unsuccessful ablation attempts using the investigational ablation system underwent attempts at ablation using an alternate system. Overall, catheter ablation was successful in 87 of 92 (95%) patients with atrioventricular nodal reentrant tachycardia, 33 of 35 (94%) patients undergoing ablation of the atrioventricular junction, and 138 of 146 (95%) patients undergoing ablation of an accessory pathway.

Relation Between Control Mode, Automatic Shutdowns, and Development of a Coagulum

The likelihood of developing a coagulum or an automatic power shutdown due to an impedance rise or an electrode temperature of >100°C (or >8° above target temperature) was related to whether radiofrequency energy was delivered in the power control mode or the temperature control mode (Table 1). Delivery of radiofrequency energy using the power control mode resulted in a greater than fivefold increase in the frequency of developing an impedance or temperature shutdown and a threefold increase in the frequency of developing a coagulum (P<.01, Table 1). One or more radiofrequency applications resulting in coagulum developed in 10 of 235 patients (4%) undergoing ablation in the temperature control mode versus 10 of 45 patients (22%) undergoing ablation in the power control mode. The probability of developing a coagulum or a temperature or impedance shutdown was related to target electrode temperature. A coagulum was observed during 0% of radiofrequency energy applications delivered with a target temperature of 70°C versus 7% of applications when the target temperature was ≥85°C (P<.001, Fig 2).

Relation Between Temperature, Ablation Target, and Ablation Approach

The mean electrode temperature achieved using closed loop temperature control was 62±12°C (range, 34° to 105°C). Electrode temperatures of ≥50°C, ≥60°C, ≥70°C, and ≥100°C were observed during 85%, 53%, 28%, and 0.6% of radiofrequency energy applications, respectively (Fig 3). The electrode temperature was >5°C lower than the targeted temperature during 60% of applications, >5°C higher than the targeted temperature during 6% of applications, and within 10°C of the targeted temperature during 34% of applications (Fig 4).
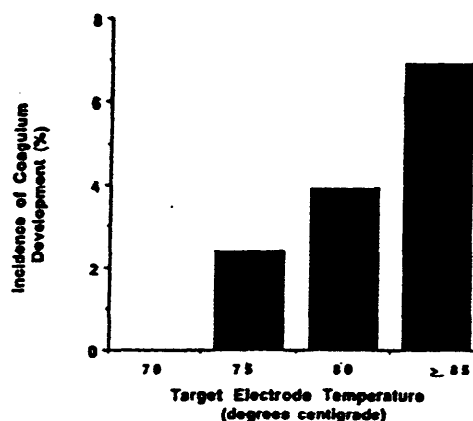

FIG 2. Bar graph showing the relation between target electrode temperature and the probability of developing a coagulum in the temperature control mode.

Electrode temperatures were related to the ablation target. Radiofrequency energy applications targeted at the atrioventricular junction resulted in the highest electrode temperatures (70±12°C), and those at sites to ablate atrioventricular nodal reentrant tachycardia resulted in the lowest (59±11°C, P=.0001, Table 2). Similarly, the difference between achieved and targeted electrode temperatures was less, and the frequency of obtaining an electrode temperature ≥50°C was greater during ablation of the atrioventricular junction than during ablation of accessory pathways or atrioventricular nodal reentrant tachycardia (P=.0001). A similar relation was observed for the frequency of achieving an electrode temperature >5°C below the targeted temperature.

During ablation of accessory pathways, electrode temperatures were related to accessory pathway location and to the approach to left free wall accessory pathways (Table 3). Electrode temperatures were highest during ablation of left free wall and posteroseptal accessory pathways and lowest during ablation of right free wall and septal accessory pathways (P<.001). Similarly, the difference between achieved and targeted electrode temperatures was less, and the frequency of achieving an electrode temperature ≥50°C was greater during ablation of left free wall and posteroseptal accessory path-
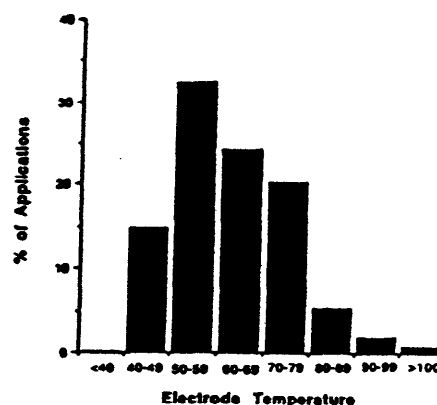

FIG 3. Bar graph showing the distribution of maximum achieved electrode temperatures during radiofrequency catheter ablation using the temperature control mode. Electrode temperature (°C) is shown on the horizontal axis; distribution of electrode temperatures is shown on the vertical axis.
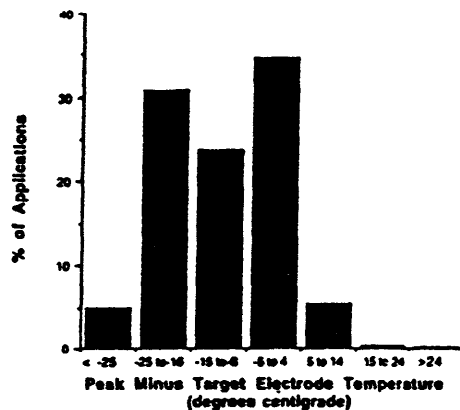
Fig 4. Bar graph showing the distribution of the difference between targeted and maximum achieved electrode temperatures (peak minus target electrode temperature) during radiofrequency catheter ablation using the temperature control mode.

ways compared with right free wall and septal accessory pathways ($P<.001$). A similar relation was observed for the frequency of achieving an electrode temperature >5°C below the targeted temperature. During ablation of left free wall accessory pathways, electrode temperatures were a mean of 8° higher using the retrograde aortic approach compared with the transseptal approach ($P<.001$, Table 3).

Relation Between Temperature and Ablation Result

Overall, no difference was observed between the electrode temperatures obtained during successful and unsuccessful applications of radiofrequency energy (64 ± 12°C versus 65 ± 13°C, $P=.8$). However, the distribution of electrode temperatures differed in that electrode temperatures of <50°C occurred more frequently during unsuccessful compared with successful applications of radiofrequency energy (16% versus 4%, $P<.001$, Fig 5). The lowest electrode temperature recorded during a successful application of radiofrequency energy was 44°C.

TABLE 2. Relation Between Electrode Temperature and Ablation Target

	Electrode Temperature (°C)	ΔT (°C)	T ≥50°C	T >(Target−5°C)
AVJ	70±12	−4±10	175/180 (97%)	114/180 (63%)
AVNRT	59±11	−13±10	539/680 (79%)	190/680 (28%)
AP	63±12	−9±10	943/1068 (87%)	483/1068 (44%)
P	.0001*	.0001*	.0001*	.0001*

AVJ indicates atrioventricular junction; AVNRT, atrioventricular nodal reentrant tachycardia; AP, accessory pathway; ΔT, difference between maximum achieved and targeted electrode temperature; T ≥50°C, frequency of achieving a maximum electrode temperature ≥50°C; T >target−5°C, frequency of achieving a maximum electrode temperature >5° below the target temperature; and electrode temperature, maximum achieved electrode temperature.

*AVJ, AVNRT, and AP are each significantly different from one another.

TABLE 3. Relation Between Electrode Temperature, Accessory Pathway Location, and Ablation Approach

Accessory Pathway Location	Electrode Temperature (°C)	ΔT (°C)	T ≥50°C	T >(Target−5°C)
RFW	58±10	13±10	217/284 (76%)	73/284 (26%)
PS	65±11	7±10	270/292 (93%)	146/292 (50%)
SEP	57±9	15±11	48/66 (73%)	18/66 (27%)
LFW	66±13	6±10	443/446 (91%)	246/446 (55%)
P	<.001*	<.001*	<.001*	<.001*
Ablation approach				
Transseptal	61±9	9±9	148/168 (88%)	80/168 (48%)
Retrograde aortic	69±14	5±10	260/278 (94%)	166/278 (60%)
P	<.001	<.001	.05	.004

RFW indicates right free wall; PS, posteroseptal; SEP, mid and anterior septal; and LFW, left free wall. Other abbreviations as in Table 2.
*PS vs LFW, $P>.05$; RFW vs SEP, $P>.05$.

Thirteen patients developed a late recurrence after catheter ablation. The electrode temperatures at the originally successful ablation sites in these 13 patients were not significantly different from the electrode temperature at successful ablation sites in the 228 patients who did not have a late recurrence (60 ± 9°C versus 64 ± 10°C, respectively, $P=.35$). The minimum electrode temperature associated with a late recurrence (48°C) was higher than the minimum electrode temperature associated with long-term success (44°C).

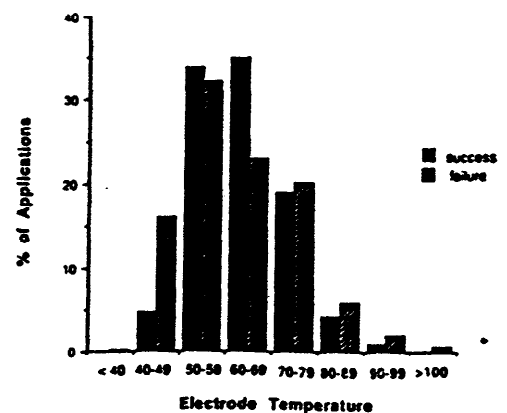The relation between electrode temperature and the ablation result during ablation of accessory pathways,

Fig 5. Bar graph showing the distribution of maximum electrode temperatures at successful and failed ablation sites. Electrode temperature (°C) is shown on the horizontal axis; distribution of electrode temperatures is shown on the vertical axis. The % of radiofrequency energy applications resulting in an electrode temperature <50°C was greater during unsuccessful compared with successful applications of radiofrequency energy.

TABLE 4. Relation Between Electrode Temperature and Ablation Result

	Electrode Temperature (°C)			ΔT (°C)			T ≥50°C			T >(Target−5°C)		
	S	F	P	S	F	P	S	F	P	S	F	P
AVJ	69±9	70±12	.51	3±8	4±10	.88	27/27 (100%)	148/153 (97%)	.99	20/27 (74%)	94/153 (61%)	.28
AVNRT	61±9	59±11	.10	11±8	13±10	.06	63/69 (91%)	476/611 (78%)	.007	18/69 (26%)	72/611 (28%)	.78
AP	64±9	63±12	.3	8±9	9±10	.63	94/97 (97%)	849/991 (86%)	.008	45/97 (46%)	38/991 (44%)	.75

S indicates successful ablation site; F, unsuccessful ablation site. Other abbreviations as in Table 2.

the atrioventricular junction, and atrioventricular nodal reentrant tachycardia is summarized in Table 4. During attempts at ablation of the atrioventricular junction, no difference was observed in any of the temperature variables at successful and unsuccessful sites, whereas during ablation of the accessory pathways and atrioventricular nodal reentrant tachycardia, the only temperature parameter that differed at successful and unsuccessful sites was the frequency of obtaining an electrode temperature ≥50°C. The relation between electrode temperature, ablation result, and the location and approach to ablation of accessory pathways is summarized in Table 5. The peak electrode temperature, the frequency of achieving an electrode temperature ≥50°C, and the frequency of achieving the target electrode temperature did not differ at successful versus failed sites during ablation of right free wall, left free wall, and posteroseptal accessory pathways. However, during ablation of septal accessory pathways, the peak electrode temperature was greater and the difference between the targeted and the achieved electrode temperature smaller at successful compared with unsuccessful sites. No difference was observed in any of the temperature

parameters at successful compared with failed sites during ablation of left free wall accessory pathways using the transseptal approach. In contrast, both the electrode temperature and the ability to achieve the targeted electrode temperature were actually lower at successful compared with unsuccessful sites during ablation of left free wall accessory pathways using the retrograde aortic approach.

Discussion

Main Findings

The purpose of the present study was to further the understanding of the role of temperature control during radiofrequency catheter ablation procedures. Important features of the ablation system used in the present study are that power output can be fixed or can be delivered in a temperature control mode, where temperature is monitored using a thermocouple incorporated into the distal electrode and power output is automatically adjusted to achieve a preset target temperature. In either mode, power output is automatically shut down if an impedance >250 Ω is detected or if the electrode temperature exceeds 100°C.

TABLE 5. Relation Between Electrode Temperature and Ablation Result During Ablation of Accessory Pathways

	Electrode Temperature (°C)			ΔT (°C)			T ≥50°C			T >(Target−5°C)		
	S	F	P	S	F	P	S	F	P	S	F	P
RFW	61±10	58±10	.08	11±2	13±10	.11	18/19 (95%)	199/265 (75%)	.053	20/27 (74%)	68/265 (28%)	.99
PS	65±7	65±11	.82	7±7	7±10	.86	22/22 (100%)	248/270 (92%)	.39	13/22 (59%)	133/270 (43%)	.51
SEP	64±9	56±9	.02	6±9	16±2	.03	8/8 (100%)	40/58 (69%)	.095	4/8 (50%)	14/58 (24%)	.2
LFW	64±10	67±13	.31	8±10	6±10	.21	46/48 (96%)	362/398 (91%)	.41	23/48	223/398 (56%)	.29
Ablation approach												
Transseptal	64±10	61±8	.28	7±10	9±9	.44	17/18 (94%)	131/150 (87%)	.7	10/18 (56%)	70/150 (47%)	.62
Retrograde aortic	64±11	70±14	.03	9±10	5±10	.03	29/30 (97%)	231/248 (93%)	.7	13/30 (43%)	153/248 (62%)	.08

Abbreviations as in Tables 2, 3, and 4.

The results of this study provide new insight into the role of closed loop temperature control during radiofrequency catheter ablation procedures. First, compared with the power control mode, in which power output is fixed, applications of radiofrequency energy delivered using the temperature control mode are associated with a threefold reduction in the incidence of developing a coagulum and a more than fivefold reduction in the incidence of developing an automatic power shutdown due to an impedance rise or an electrode temperature >100°C. Second, in the temperature control mode, targeted temperatures are achieved (±5°C) during only one third of radiofrequency energy applications when the maximum available power is 50 W. Third, the temperature achieved in the temperature control mode is related to the ablation target, with ablation of the atrioventricular junction resulting in the highest temperatures and ablation of atrioventricular nodal reentrant tachycardia the lowest. During ablation of accessory pathways, ablation of left free wall and posteroseptal accessory pathways results in higher electrode temperatures than those achieved during ablation of right free wall and septal accessory pathways. Finally, for all ablation sites, the temperature of the applications of radiofrequency energy that result in successful ablation are not significantly different from those that fail. In fact, while a mean of 64±12°C was recorded from successful ablation sites, successful ablation could be achieved with the electrode tip temperature as low as 44°C. Although electrode temperature differences between successful and failed applications of radiofrequency energy are present only during ablation of septal accessory pathways, temperature alone was clearly not the main determinant of success, since electrode temperatures were actually lower at successful sites than unsuccessful sites during ablation of left-sided accessory pathways using the retrograde approach (Table 5).

Coagulum Formation

Temperatures >100°C result in tissue desiccation and the development of a coagulum on the ablation electrode.[8] Although not usually harmful to the patient, they are undesirable during ablation procedures because they result in an abrupt rise in impedance and fall in current density at the electrode-tissue interface that impairs further heating required for maximizing lesion size. In addition, the ablation catheter must be extracted and the coagulum removed from the electrode tip. This requires additional catheter manipulation and additional fluoroscopy time. Finally, a coagulum may be loosely adherent to the electrode and potentially dislodge from the catheter tip, resulting in a vascular embolus, or may cause the electrode tip to adhere to the tissue.

A potential benefit of closed loop temperature control is that temperatures approaching 100°C can be avoided, thereby maximizing lesion size while preventing the development of a coagulum. However, it should be noted that closed loop temperature control did not eliminate the development of all coagulum. The probability of developing a coagulum increased progressively as the target electrode temperature was increased from 70°C to >85°C. These findings may reflect both a slight delay inherent in any feedback control system as well as the location of the thermocouple within the ablation electrode.

Temperature Monitoring During Radiofrequency Catheter Ablation

Temperature monitoring was performed in this study using a thermocouple incorporated into the distal electrode of the ablation catheter. During delivery of radiofrequency energy, a portion of the electrode is typically in contact with the myocardium and the remainder in contact with the blood pool. The electrode temperature recorded by the thermocouple reflects a complex interaction between the production of heat in nearby tissue by the radiofrequency field and convective heat loss to the surrounding blood and tissue.[5-7,10]

This study demonstrates that despite the presence of closed loop feedback control and a maximal power output of 50 W, targeted electrode temperatures (±5°C) are achieved during only one third of radiofrequency energy applications. Although the basis for this inability to achieve targeted temperatures cannot be determined from the results of this study, it may reflect relatively large contact of the electrode tip with blood compared with tissue. Heat generation during radiofrequency catheter ablation results from resistive heating of myocardium and is dependent on current flow through the tissue.[5,6] Because the impedance of the blood is significantly lower than that of tissue,[11] relatively more contact with the blood compared with the myocardium would be expected to result in greater convective heat loss to the surrounding moving blood, which is relatively cooler. Reduced tissue contact may be either the result of the orientation of the catheter tip to the anatomic structure it impinges on or catheter instability with electrode movement on and off the tissue.

The electrode temperature achieved during applications of radiofrequency energy in this study varied with the ablation target, being highest during ablation of the atrioventricular junction and lowest during ablation of atrioventricular nodal reentrant tachycardia. During ablation of accessory pathways, electrode temperatures were greater for left free wall and posteroseptal accessory pathways than for right free wall and septal accessory pathways. These differences may reflect target-dependent differences in electrode-tissue contact, catheter stability, and/or convective heat loss to the blood pool. Catheter positioning in the region of the His bundle is easily accomplished and may allow greater catheter torque with better electrode-tissue contact and catheter stability compared with catheter positions along the inferior septal region of the tricuspid annulus. Similarly, the catheter positions used during ablation of posteroseptal and left free wall accessory pathways generally result in more stable catheter contact with less exposure to high velocity blood flow compared with those used for ablation of right free wall, mid, and anterior septal accessory pathways. The higher electrode temperatures achieved during ablation of posteroseptal accessory pathways compared with sites for cure of atrioventricular nodal reentrant tachycardia may similarly reflect differences in catheter stability. Although the catheter is positioned along the inferior tricuspid annulus for both ablation targets, the catheter is typically positioned on the ventricular side of the annulus (larger ventricular than atrial electrogram) for ablation of atrioventricular nodal reentrant tachycardia,

which generally results in greater catheter instability. The observed difference between left free wall accessory pathways ablated using the transseptal versus the retrograde aortic approach can be similarly explained.

lectrode placement on the atrial side of the mitral annulus generally results in greater catheter instability and possibly greater surrounding blood flow compared with the retrograde aortic approach, where the ablation catheter is generally positioned firmly under the mitral annulus in a region that may be associated with less convective heat loss.

In this study, the minimal temperature associated with success was 44°C. Whereas 50°C has been demonstrated to be the temperature at which irreversible tissue injury occurs in vitro,[4] the lower recorded-electrode temperature in this study may be explained in part on the location of the thermocouple within the ablation electrode. As outlined previously, heating of the electrode results from passive heat transfer from the electrode-tissue interface. Because of convective heat loss to the surrounding blood pool, the temperature recorded by the thermocouple should be consistently less than that at the hottest point in the tissue. Blouin et al[10] compared temperature monitoring using a thermistor positioned on the tip of an electrode catheter at the electrode-tissue interface with temperature monitoring using a thermistor incorporated into the distal electrode. The temperature differential was highly predictable in that the temperature sensed by the internally mounted thermistor was consistently lower than that at the electrode-tissue interface (mean difference, 5°C: range, 2° to 8°C). Thus, a 44°C temperature recorded from a thermocouple incorporated into the distal electrode in this study may reflect a significantly higher temperature at various points in the tissue. The mean electrode temperature at successful ablation sites was 64±12°C. Using the data of Blouin et al,[10] this could reflect a temperature at the electrode-tissue interface of approximately 70°C.

An application of radiofrequency energy may be unsuccessful due to inadequate tissue heating or incorrect catheter positioning. Lower electrode temperatures at unsuccessful versus successful sites was observed only during ablation of septal accessory pathways. The absence of a temperature difference at successful (with or without late recurrence) versus failed sites during ablation of the atrioventricular junction, atrioventricular nodal reentrant tachycardia, and most accessory pathways suggests that incorrect catheter positioning rather than inadequate tissue heating may have been the reason for failure. In support of such a hypothesis, temperatures were actually higher at failed than at successful sites using a retrograde aortic approach to left-sided pathways. Although this finding may have been due to chance, it may also reflect generation of higher temperatures when the catheter tip is lodged in a ventricular trabecula away from the atrioventricular groove than when it is at the smooth annulus under the mitral valve. The absence of a difference in electrode temperature at all successful and failed sites may also reflect the presence of closed loop temperature control, which will minimize temperature differences by automatically adjusting the power at any site. The lower temperature at unsuccessful sites of radiofrequency energy delivery during ablation of septal accessory

pathways suggests that inadequate heating may be the limiting factor for this ablation target.

Comparison With Prior Studies

The value of temperature monitoring has been appreciated for more than 30 years.[5,12,13] More recently, the role of temperature monitoring during cardiac radiofrequency catheter ablation procedures has been evaluated in the experimental laboratory.[7-9] These studies demonstrated that electrode temperature is a better predictor of lesion size than delivered power, current, or energy and defined 100°C as the temperature above which tissue contiguous to the electrode desiccates, resulting in the development of a coagulum. Only one prior study by Langberg et al[14] has evaluated the role of temperature monitoring during radiofrequency catheter ablation procedures in humans. This study differed from the present study in many respects: (1) electrode temperatures were only evaluated during catheter ablation of accessory pathways; (2) at each ablation site, successive applications of radiofrequency energy were delivered at increasing power; (3) electrode temperature was monitored using a thermistor located at the tip of the ablation catheter and thermally insulated from the surrounding electrode; (4) temperature was monitored but was not used to control power output; and (5) catheter ablation of left free wall pathways was performed using only the retrograde aortic approach. Despite these differences, the minimum and mean temperatures reported by Langberg et al at successful ablation sites (48°C and 62±15°C, respectively) were similar to those reported in this study (44°C and 64±12°C, respectively). The slightly lower minimum successful temperature in this study may reflect the location of the thermocouple within the ablation electrode. Both studies also demonstrated that radiofrequency energy applications on the atrial side of the tricuspid annulus result in lower temperatures than do applications on the ventricular side of the mitral annulus (retrograde aortic approach).

Although the site of temperature monitoring within the ablation electrode differed in these two studies, the results do not allow us to determine which is preferable. One potential advantage of a thermistor on the catheter tip is that it is an accurate representation of the temperature at the electrode-tissue interface, provided that the electrode is perpendicular to the myocardium.[14,15] However, the relation between electrode temperature and that at the electrode-tissue interface is dependent on the orientation of the electrode, with differences as great as 12°C being observed if the electrode is parallel to the myocardium.[15] A limitation of temperature monitoring using a thermocouple incorporated into the electrode is that convective cooling results in consistently lower temperatures than occur at the electrode-tissue interface. However, an internally positioned thermocouple may be less dependent on electrode orientation relative to the myocardium and may be a preferable approach to controlling power output.

Study Limitations

A limitation of this study is that the incidence of complications resulting from radiofrequency energy delivery during ablation procedures is exceedingly low,

and a relatively small number of patients had catheter ablation performed with a preset fixed power output. Therefore, the results of this study do not allow us to determine if the temperature control mode results in improved safety and efficacy of radiofrequency catheter ablation procedures.

Clinical Implications

The results of the present study suggest that closed loop control of power output to achieve target electrode temperatures may facilitate radiofrequency catheter ablation of accessory pathways, atrioventricular nodal reentrant tachycardia, and the atrioventricular junction. Although a potential benefit of closed loop temperature control is that power is automatically adjusted in an attempt to achieve preset electrode temperatures, target electrode temperatures were achieved in only one third of radiofrequency energy applications using a maximum power output of 50 W. This finding suggests that catheter tip–tissue contact continues to be an important clinical problem that cannot be overcome with closed loop control and will require improvements in catheter design, ablation technique, or perhaps an energy source not dependent on catheter-tissue contact. Closed loop control appears to be effective in reducing the incidence of developing a coagulum on the ablation electrode, particularly for target electrode temperatures of ≤75°C. Further studies will be required to determine whether closed loop control improves the safety and efficacy of radiofrequency catheter ablation procedures.

Appendix

Atakr Investigators and Institutions

G. Neal Kay, MD; Sharon Dailey, MD: Andrew Epstein. MD; Vance Plumb, MD; University of Alabama at Birmingham, University Hospital, Birmingham, Ala; Marcus Wharton. MD; Ronald Kanter, MD; Robert Sorrentino, MD; Ruth Ann Greenfield, MD; Duke University Medical Center, Durham. NC; Edward Walsh, MD; Children's Hospital, Boston, Mass: Albert Waldo, MD; Lee Biblo, MD; Nancy Johnson, MD: Randy Lieberman, MD; David Rosenbaum, MD; University Hospital of Cleveland (Ohio); S.K. Stephen Huang, MD; Robert S. Mittleman, MD; Alan B. Wagshal, MD; Trevor Greene, MD; University of Massachusetts Medical Center, Worchester; Bing Liem, DO; Michael Lauer, MD; Ruey Sung, MD; Charlie Young, MD; Stanford University Medical Center, Stanford, Calif; Joseph Evans, MD; Northside Cardiology, Indianapolis, Ind; Christopher Case, MD; Medical University of South Carolina, Charleston; Kevin Hackett, MD; William Miles, MD; Douglas Zipes, MD; Krannert Institute, Indianapolis, Ind; Jack Lawrence, MD; Gordon Tomaselli, MD; Ronald Berger, MD; Johns Hopkins Hospital, Baltimore, Md.

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Closed Cooled Ablation for the Treatment of Atrial Flutter

S. G. Spitzer, H. H. Ebert, L. Karolyi, P. Richter

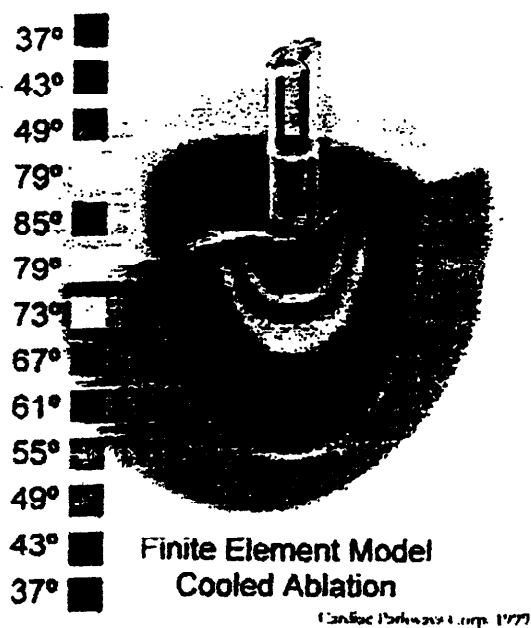Dresdner Institut für Herz- und Kreislaufforschung e. V., Dresden, Germany

Radiofrequency (RF) catheter ablation is highly effective and safe in the curative treatment of many cardiac arrhythmias. High success rates (greater than 90 %) have been reported in treating supraventricular tachycardias (SVT) and idiopathic ventricular tachycardias (VT).

Lesions of adequate size are necessary to irreversibly interrupt the conduction through an abnormal pathway or to destroy a focus of automaticity.

Radiofrequency energy is directed between an electrode tip on the endocardial surface and an electrode pad on the patient's skin. Lesions are created by resistive heating in the tissue in contact with the electrode tip and conductive heating in the area more distant from the tip. The typical diameter of a lesion measures 4 to 5 mm, the depth 3 mm. Lesion size depends on tip temperature, applied power and the duration of energy delivery. In a less degree it depends on electrode size, tissue impedance, contact pressure, convective heat loss and catheter tip angle.

Lesions may not reach intramyocardial or epicardial foci. Scar tissue is not readily penetrated. Repeated RF discharges prolong the duration of the procedure and increase the extent of healthy tissue damage.
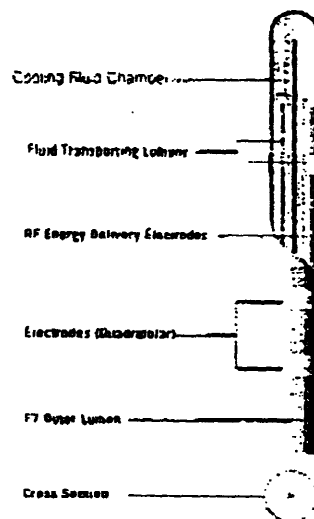Catheter electrode temperatures above 100 degrees C result in coagulum formation at the electrode-tissue interface leading to sudden impedance rise and significant loss in the power delivered.

37°
43°
49°
79°
85°
79°
73°
67°
61°
55°
49°
43° Finite Element Model
37° Cooled Ablation

Cardiac Pathways Corp. 1997

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Cooling Fluid Chamber

Fluid Transporting Lumen

RF Energy Delivery Electrodes

Electrodes (Bipolar)

F7 Outer Lumen

Cross Section

The ideal ablation device should allow the creation of large and deep lesions in a safe manner (no coagulum, no perforations, etc). Lesion size and shape should be titratable. Further, it should be economically feasible.

Saline infusion systems can potentially overcome some of the limitations of classic RF catheters by cooling the catheter tip. Cooled catheter tips allow greater energy delivery without exceeding 100 degrees C at electrode-tissue interface and hence greater lesion volumes and fewer impedance rises. The center of maximal heating moves deeper into myocardium. An important trade-off is the loss of meaningful temperature measurement, since temperature is measured on the surface.
There are two types of cooled RF catheters: catheters with lumens can irrigate saline directly onto myocardium, closed loop catheters can recirculate saline within the catheter to the tip.

Several studies using both conventional and cooled tip RF ablation have shown that the tip temperature provides an efficient indicator of lesion growth [1,2]. Temperature values at the catheter tip are typically kept within 60-70°C for conventional RF ablation, while for the cooled tip ablation these target values are markedly lower due to the tip cooling process. Experimental and clinical data for cooled tip ablation suggest that the optimal tip temperature range is 40-45°C, which can be usually achieved by titration of power levels at a continuous delivery of 30-35 Watts. However, when the contact between the tip of the catheter and viable myocardial tissue is poor, the tip temperature remains below 36°C and does not change with increasing power levels. Such low temperatures may also be recorded when the tip of the catheter is in contact with infarcted tissue or when the catheter tip is unstable due to a rapid cardiac rate.

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CPC has developed a 7F deflectable quadrapolar catheter with closed-loop cooling lumens through which saline solution (at room temperature) is circulated through the tip under a constant volumetric flow rate using an injector pump. Temperature of the 4-mm long catheter tip is monitored with a thermocouple embedded just proximal to the inside edge of the tip. While the internal saline solution cools the catheter tip, RF current is delivered using a computer-controlled generator that produces up to 50 Watts of power and provides continuous digital and/or graphical display of system power, impedance, current, voltage, and tip temperature.

Typical atrial flutter (AF) is a macroreentrant tachycardia propagating counterclockwise or, less commonly, clockwise in the right atrium. Catheter ablation using RF energy with the endpoint of a bi-directional isthmus conduction block is a very effective treatment option. Recent data indicates that RF ablation incorporating an irrigation tip to provide cooling is effective in patients in whom conventional RF ablation is ineffective [10]. This type of catheter is generally recommended for ablation in the ventricle. It is possible that a catheter incorporating distal cooling, which allows greater energy delivery and increased lesion volume, may be more effective in treating AF.

This study sought to proof that primary isthmus ablation using the closed circuit cooled tip catheter to create bi-directional block is feasible and safe.

Ablation of typical AF was performed in 30 patients between 12 / 98 and 05 / 99 by using a cooled ablation system utilizing a closed path fluid circulation to control the tip temperature during ablation (Chilli Cooled Ablation Catheter, Cardiac Pathways Corp.). A series of RF applications was applied on the isthmus between the tricuspid valve annulus and the inferior vena cava. Bidirectional block was confirmed by complete clockwise isthmus block during proximal coronary sinus pacing and counterclockwise isthmus block during low lateral right atrial pacing.

Number of patients	30
Gender male – female	23 – 7
Age	60.9 ± 11.4 years
Number of RF applications	14.3 ± 7.8
Power	35 to 50 watts
Tip temperature	38 to 43 degrees C
Application duration	9.9 ± 5.3 min
Energy used	25053 ± 14949 watts x sec
Procedure time	75.9 ± 22.9 min
Fluoroscopy time	19.1 ± 8 min

No additional conventional RF ablations were applied. Complete bidirectional block was confirmed in all patients. One patient with difficult anatomical conditions showed a small pericardial effusion without hemodynamic consequences. All patients were in sinus rhythm at hospital discharge.

Primary cooled tip ablation of typical atrial flutter using a closed catheter with distal cooling is feasible and can be performed safely and effectively.

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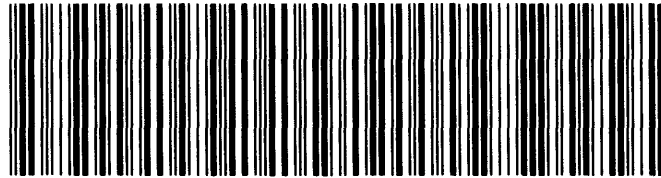**PRIORITY OVERNIGHT   THU.**

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